

REMARKS

Claims 1-14 and 18-43 are pending in the present application. Claims 2, and 13 have been amended. Support for the amendments is found throughout the specification. No new matter has been added by virtue of these amendments and their entry is respectfully requested. Amendment and cancellation of the claims are not to be construed as an acquiescence to any of the rejections/objections set forth in the instant Office Action, and were done solely to expedite prosecution of the application. Applicants reserve the right to pursue the claims as originally filed, or substantially similar claims, in this or one or more continuation patent applications.

Claim Rejections Under 35 U.S.C. § 112.

Claims 2, 13-14 and 18 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 was subject to a restriction requirement and has now been reinstated by the Examiner. In response, Applicants have amended claim 2 to substitute the term "marker" and replacing the term with "protein" so as to provide the correct antecedent basis. The term "analyzing" was replaced by the term "contacting" so as to provide the correct antecedent basis. Claim 13 was amended to add further clarify that detecting overexpression of VEGF-D in the brain tissue sample comprises the step of "contacting" at least a portion of said brain tissue sample with a probe that specifically binds to the VEGF-D protein. See, for example, page 2, lines 11-18; page 2, lines 26-29. These amendments are made solely for expediting prosecution and are not meant to be construed as surrender of any subject matter.

In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

Claim Rejections Under 35 U.S.C. § 103.

Claims 1, 9-11 and 13-14 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Takano et al (Cancer Research 56:285-2190, May 1996; PTO 1449) as evidenced by Amalfitano *et al.*, (Cancer Genet Cytogenet 116:6-9, 2000; PTO 892) in view of Achen et al (Eur. J. Biochem. 267:2505-2515, 2000; PTO 1449) and US Pat No. 6,235,713 B1.

Applicants respectfully disagree and traverse the rejection.

Takano et al., discuss VEGF in the sera and tumor extracts of patients. Takano *et al.*, indicate that VEGF₁₂₁ is freely soluble and there appears to be poor cross reactivity between any other forms of VEGF. This shown in Figure 2 where the anaplastic astrocytoma also stained highly positive. (See, also Table 1). Applicants respectfully disagree with the Examiner's assertions that Takano et al., taken in view of Amalfitano *et al.*, and Achen et al make the instant invention obvious. The highly cross reactive antibody is by no means a method of identifying a glioblastoma as in the instant invention. The motivation does not exist in any of the cited to combine the references. As discussed, Takano et al., do not teach or disclose detection of VEGF-D by a labeled antibody in a brain sample. Amalfitano *et al.*, do not teach the detection of full-length native VEGF-D in brain tissue samples. Achen et al, standing alone or in combination do not teach the detection of a native protein VEGF-D homology domain in brain cancer. None of the references teach the detection of VEGF-D in the brain nor, was the form of VEGF-D in the brain known prior to applicants invention. The motivation to combine these references is not provided by the references.

In view thereof, Applicants respectfully request reconsideration and withdrawal of the rejection.

CONCLUSION

Applicants respectfully request entry of the foregoing remarks and reconsideration and withdrawal of all rejections. It is respectfully submitted that this application with claims 1, 9, 10

and 12-18 define patentable subject matter and is in condition for allowance. Accordingly, Applicant respectfully requests allowance of these claims.

Applicants have made every effort to present claims which distinguish over the cited art, and it is believed that all claims are now in condition for allowance. However, Applicants request that the Examiner call the undersigned (direct line 561-671-3666) if anything further is required by the Examiner prior to issuance of a Notice of Allowance for all claims.

This response is being filed within the shortened statutory period and as such no extension of time or fees are due. Although, Applicants believe that no extensions of time or fees are due, please consider this submission as a petition for any retroactive extension of time needed. The Commissioner for Patents and Trademarks is hereby authorized to charge the amount due for a one month retroactive extension of time and any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees paid on the filing, or during prosecution of this application to Deposit Account No. 50-0951.

Respectfully submitted,

AKERMAN SENTERFITT



Nicholas A. Zachariades, Ph.D.
Reg. No. 56,712
222 Lakeview Avenue, Suite 400
West Palm Beach, FL 33401-6147
Tel: (561) 653-5000

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